# Biomarker Relatability in the International Severe Asthma Registry

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## Introduction

- Inflammatory biomarkers are useful to phenotype patients with severe asthma and guide targeted therapies.
- Little is known about the overlap and relatability of positive biomarkers in severe asthma.
- This study describes the point prevalence, overlap, and relatability of three commonly used asthma biomarkers:
  - Total serum immunoglobin E (IgE)
  - Blood eosinophil count (BEC)
  - Fractional exhaled nitric oxide (FeNO)

## Methods

- This cross-sectional study included adults with severe asthma enrolled in the International Severe Asthma Registry (ISAR)[1–4] with baseline measurement of all three biomarkers.
- Cut-off points for positivity were pre-defined as follows: IgE ≥ 75kU/L, BEC ≥ 300 cells/uL, FeNO ≥ 25ppb.
- Where possible, biomarkers were measured prior to biologic therapy initiation; however, some patients were on biologics at registry entry.
- Point prevalence for each group was described.
- For each biomarker, the percent likelihood for alternative biomarker positivity was calculated.

### Patients included

- Patients in ISAR are aged ≥ 18 years, received treatment at Global Initiative for Asthma (GINA 2018) Step 5, or had uncontrolled asthma (i.e., severe symptoms or frequent exacerbations) at GINA 2018 Step 4 (at inclusion),[3] and
- Provided consent for their prospective data to be included, and
- Had all three biomarkers (IgE, BEC, FeNO) measured at baseline.

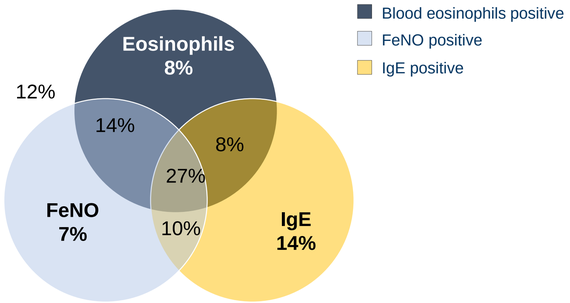
## Results

- A total of 1175 adult patients with severe asthma from 10 countries were included in the analysis (17% of the total ISAR cohort).
- 64% of patients were female, mean ± SD age 53 ± 15 years, BMI 30 ± 8, post-bronchodilator forced expiratory volume in one second ($FEV_1$) 2.2 ± 0.8 litres, and 74 ± 20% predicted.

### Point prevalence of biomarker groups

- Overall, 59% of patients were IgE positive, 57% eosinophil positive, and 58% FeNO positive.
  - Overlap of the three groups is shown in ***Figure 1***.
- The largest group was triple biomarker positive (27%).
  - Triple-positivity was 44% in patients treated with oral corticosteroids.
- Other groups were:
  - IgE positive 14%,
  - eosinophil/FeNO positive 14%,
  - triple negative 12%,
  - eosinophil/IgE positive 8%,
  - FeNO/IgE positive 10%,
  - eosinophil positive 8%, and
  - FeNO positive 7%.

**Figure 1:** Overlap of biomarker positivity in the International Severe Asthma Registry cohort (n=1,175)



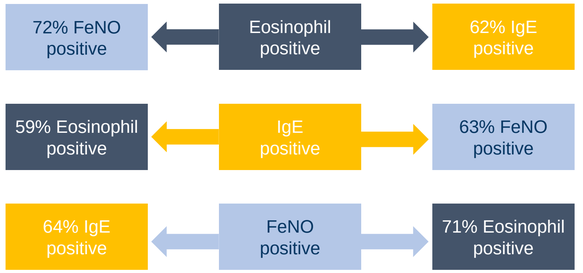

Abbreviations: FeNO, fractional exhaled nitric oxide; IgE, immunoglobulin E

## Results

### Likelihood for alternative biomarker positivity

- In patients with eosinophil positivity, 72% also had FeNO positivity, and 62% also had IgE positivity
- In patients with IgE positivity, 59% also had eosinophil positivity, and 63% also had FeNO positivity
- In patients with FeNO positivity, 64% also had IgE positivity, and 71% also had eosinophil positivity (***Figure 2***).

**Figure 2:** Percentage of other biomarkers positive when one is positive based on dichotomous cutoffs as follows: IgE ≥ 75kU/L, BEC ≥ 300 cells/uL, FeNO ≥ 25ppb.




Abbreviations:
BEC, blood eosinophil count;
FeNO, fractional exhaled nitric oxide;
IgE, immunoglobulin E

## Conclusions

- **In this large international severe asthma cohort, most patients were positive for at least one potentially actionable biomarker at baseline, similar to findings in a general asthma population.[5]**
- **Overlap appeared to be greater between eosinophil and FeNO positivity than with IgE positivity.**
- **The considerable overlap in biomarker positivity suggests that more than one targeted therapy may be suitable for many patients with severe asthma.**
- **There was a small triple negative group suggesting heterogeneity of underlying pathogenesis.**

## References

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